

- ai coner*
- (c) determining whether the neuromuscular phenotype is modulated by the putative agent, thereby identifying an agent capable of modulating the neuromuscular phenotype.
-

Please add new claims 21-30 as follows:

21. (New) A transgenic mouse comprising a disruption in an endogenous NPY6 gene that results in loss of function of NPY6, wherein where the disruption is homozygous, the transgenic mouse exhibits, relative to a wild-type mouse, a neuromuscular phenotype.

as

22. (New) The transgenic mouse of claim 21, wherein the neuromuscular phenotype comprises increased coordination or increased agility.

23. (New) The transgenic mouse of claim 22, wherein the increased coordination or increased agility is characterized by an increased latency to fall off of an accelerating rotarod.

24. (New) A cell obtained from the transgenic mouse of claim 21.

25. (New) A method of producing a transgenic mouse comprising a disruption in an endogenous NPY6 gene, the method comprising:

- (a) introducing an NPY6 gene targeting vector into a murine embryonic stem cell;
- (b) introducing the cell into a blastocyst;
- (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and
- (d) breeding the chimeric mouse to produce the transgenic mouse,

wherein the disruption results in loss of function of NPY6 and, where the disruption is homozygous, the mouse exhibits, relative to a wild-type mouse, a neuromuscular phenotype.

26. (New) A targeting vector comprising:

- (a) a first polynucleotide sequence homologous to a first region of an endogenous NPY6 gene;

- (b) a second polynucleotide sequence homologous to a second region of the endogenous NPY6 gene; and
- (c) a selectable marker located between the first polynucleotide sequence and the second polynucleotide sequence,

wherein the targeting vector, when introduced into a murine embryonic stem cell, results in a transgenic mouse having a disruption in the endogenous NPY6 gene, wherein the disruption results in loss of function of NPY6 and, where the disruption is homozygous, the mouse exhibits a neuromuscular phenotype, relative to a wild-type mouse.

27. (New) A murine cell transformed with the targeting vector of claim 26.
28. (New) A murine embryonic stem cell comprising a disruption in an endogenous NPY6 gene, the disruption produced using the targeting vector of claim 26.
29. (New) A method of producing a targeting vector capable of disrupting an endogenous NPY6 gene, the method comprising:
- (a) providing a first polynucleotide sequence homologous to a first region of an endogenous NPY6 gene;
 - (b) providing a second polynucleotide sequence homologous to a second region of the endogenous NPY6 gene;
 - (c) providing a vector comprising a selectable marker; and
 - (d) inserting the first and second sequences into the vector such that the selectable marker is located between the first and the second sequences to produce the targeting vector,
- wherein the targeting vector, when introduced into a murine embryonic stem cell, results in a transgenic mouse having a disruption in the endogenous NPY6 gene, wherein the disruption results in loss of function of NPY6 and, where the disruption is homozygous, the mouse exhibits a neuromuscular phenotype, relative to a wild-type mouse.
30. (New) A method of producing a targeting vector capable of disrupting an endogenous

NPY6 gene, the method comprising:

- (a) providing a polynucleotide sequence homologous to at least a portion of an endogenous NPY6 gene;
 - (b) generating two different fragments of the polynucleotide sequence;
 - (c) providing a vector having a gene encoding a selectable marker; and
 - (d) inserting the two different fragments into the vector such that the selectable marker is located between the two different fragments to produce the targeting vector,
- wherein the targeting vector, when introduced into a murine embryonic stem cell, results in a transgenic mouse having a disruption in the endogenous NPY6 gene, wherein the disruption results in loss of function of NPY6 and, where the disruption is homozygous, the mouse exhibits a neuromuscular phenotype, relative to a wild-type mouse.

a2
con